IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	
Gunji et al.	Art Unit: 1652
Application No.: 10/716,480	Examiner: Robinson
Filing Date: November 20, 2003	Attorney Ref. No.: US-102
For: METHOD FOR PRODUCING L-AMINO ACID USING METHYLOTROPH	**VIA EFS-WEB**

REPLY BRIEF FOR APPELLANT

Mail Stop Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

COMES NOW the Appellant to present this Reply Brief in support of the appeal of the final rejection of Claims 2-4 and 6-7 contained in the Office Action dated May 23, 2005 ("Final Rejection"), and to respond to the Examiner's Answer dated February 23, 2006 in the above-captioned patent application. A petition for an extension of time is not necessary, as this Reply Brief is being filed within two months of the mailing of the Examiner's Answer.

It is not believed that extensions of time are required, beyond those that may otherwise be provided for in accompanying documents. If, however, additional extensions of time are necessary to prevent abandonment of this application or dismissal of this appeal, then such extensions of time are hereby petitioned under 37 C.F.R. § 1.136(a), and the Commissioner is hereby authorized to charge fees necessitated by this paper, and to credit all refunds and overpayments, to deposit account 50-2821.

For the following reasons, Appellant respectfully submits that the final rejection of each of Claims 2-4 and 6-7 in this application is in error, and therefore respectfully requests reversal of the rejections.

I. Real Party in Interest

See Appeal Brief filed December 15, 2005.

II. Related Appeals and Interferences

See Appeal Brief filed December 15, 2005.

III. Status of Claims

See Appeal Brief filed December 15, 2005.

IV. Status of Amendments

See Appeal Brief filed December 15, 2005.

V. Summary of Invention

See Appeal Brief filed December 15, 2005.

VI. Issues

See Appeal Brief filed December 15, 2005.

VII. Grouping of Claims

See Appeal Brief filed December 15, 2005.

VIII. Argument

In the Examiner's Answer dated 23 February 2006, beginning at page 3, Claims 2-4 and 6-7 were rejected under 35 U.S.C. § 112, 1st paragraph, because the specification, while being enabling for a DNA of SEQ ID NO. 1, in which a mutation results in glycine residue 56 being replaced by serine, allegedly does not reasonably provide enablement for the genus of any DNA that encodes a mutant LysE protein of a coryneform bacteria. For at least the following reason, this rejection is in error and should be reversed.

The Examiner has made several statements and attempted to advance several lines of argument that are addressed herein. On page 7, the Examiner states that no correlation is made between structure and function for the variants encompassed by the claims.

However, this is entirely false. Firstly, the information about the LysE sequence from other bacteria, even those as diverse as *E. coli,* was known in the art. Knowledge of these sequences provides a wealth of structure-function relationship information. Therefore, combined with the information provided in the specification, clearly sufficient structure-function information has been provided to allow one of skill in the art to determine other mutational species of these proteins which will retain the claimed function, particularly when the variance permitted by the claim is so small – the variance allowed by the scope of the claims is a mere 4.2% (10 amino acid residues/ 236 amino acid residues).

The Examiner's statement on page 8 that the mutations which fall within the scope of the claim are "randomly selected" (see 1st line on page 8) is also entirely false. Mutations in the LysE protein are not randomly selected, but are based upon much information in the prior art and Appellant's specification regarding the sequence and the protein's function, the mutations presented in the specification's examples, and the knowledge in the art about LysE from other species, and the conserved and non-conserved residues between such proteins. All of this information provides the skilled art worker with sufficient guidance for **carefully selecting** mutations which fall within the scope of the claims (a mere 4.2% variance in sequence from SEQ ID No. 2), and being able to predict maintaince of claimed resistance to S-(2-aminoethyl)cysteine.

In addressing Appellant's submitted alignment data, which is completely summarized in the Appeal Brief, the Examiner states that this data is "not representative of the entire genus encompassed in the claimed invention", and that sequence homology does not indicate where in a sequence "all the variants encompassed in the claims can be made or predict function". Appellants submit that neither of these statements refects the correct standard for undue experimentation. The entire genus does not need to be exemplified, or even represented by the submitted data; however, the data should and does demonstrate the routineness for the person of ordinary skill in the art for **predicting** residues which may be mutated within the scope of the claims, which is the proper standard for evaluating undue experimentation. The alignment data clearly show conserved regions among the family of LysE proteins, and non-conserved regions. One of ordinary skill in the art would be able to reasonably predict that mutations made in the conserved regions might adversely effect the function, whereas mutations made in the non-conserved regions might not effect function.

On page 10, the Examiner states that "no conserved region is identified." Such a statement is directly counter to the evidence presented on the record. As stated above, conserved and non-conserved regions are shown in the attached alignments, and clearly provide information to the skilled art worker as to which residues can be mutated or not mutated within the scope of the claims. Furthermore, based on the above statement that "no conserved regions is identified", the Examiner proceeds to make the entirely false assumption that any 10 residues at any positions other than 56 can be deleted, substituted, or inserted, and then calculates the combinatorials possible based upon these false assumptions, which of course, results in an impossible number of possibilities. Such a calculation entirely distorts the reality of the situation, resulting in a meaningless number.

Actually, many of the possibilities encompassed by the Examiner's calculation would not even be considered by the skilled artisan since the skilled artisan would know that mutations should be made outside the conserved regions or at a non-conserved residue (as shown in the alignment data), conservative subsitutions may be made even outside the conserved regions or at non-conserved residues, or large (over 10) numbers of amino acids should not be deleted from a conserved region, etc.. The Examiner's calculation totally ignores the wealth of knowledge in the art about LysE, its sequence and structure, its function and activity, common knowledge in the art concerning amino acid mutations, and the submitted alignment data showing the knowledge in the art about the family of LysE proteins and their structures. Such knowledge and data cannot be ignored when evaluating undue experimentation (*see In re Wands* 858 F.2d 731 (Fed. Cir. 1988)); however, the Examiner's caluclation does just that.

The Examiner states on page 8 that "the skilled artisan would recognize the high degree of unpredictability that **all** the variants encompassed in the claims would retain the recited function/activity." Actually, the claim only encompasses variants or mutants which impart resistance to S-(2-aminoethyl)cysteine. The Examiner seems to be stating that her combinatorial calculation should result in the number of variants which do retain such activity, which is clearly incorrect. Again, one of ordinary skill in the art clearly possesses sufficient information to be able to reasonably predict variants which might retain this activity, which is clearly a number far less than the number determined by the Examiner, based upon the known LysE sequence and the known sequences of the LysE

family members.

On a final note about the alignment data, , the Examiner actually suggested the submission of such data in order to demonstrate that one of ordinary skill in the art would be able to routinely determine substitutions, deletions, or insertions without changing the ability of the protein to impart resistance to S-(2-aminoethyl) cysteine. Although this telephone interview was not 'on the record', it was memorialized on page 5 of the response filed September 20, 2005.

For at least the reasons presented herein, each of the subject matters of Claims 2-4 and 6-7, taken as a whole, are patentable and meet the enablement requirement of 35 U.S.C. §112, 1st paragraph. Accordingly, the rejection of each of Claims 2-4 and 6-7 under section 112, 1st paragraph is reversible error.

IX. Conclusion

For at least the foregoing reasons, Appellant respectfully submits that the subject matters of Claims 2-4 and 6-7, each taken as a whole, are patentable. Accordingly, Appellant respectfully requests reversal of the rejections of Claims 2-4 and 6-7 under section 112, 1st paragraph.

Respectfully submitted,

By: _____
Shelly Guest Cermak
Registration No. 39,571

U.S. P.T.O. Customer Number 38108
Cermak & Kenealy LLP
515 East Braddock Road, Ste. B
Alexandria, VA 22314
703 778 6608
703 652 5101 (fax)
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